NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

OYSTER POINT PHARMA, INC., Plaintiff, v. APOTEX INC., Defendant.	**Civil Action No. 23-3860 (SRC)** **OPINION & ORDER**

CHESLER, U.S.D.J.

This matter comes before the Court on the application for claim construction by Plaintiff Oyster Point Pharma, Inc. ("Oyster Point") and Defendant Apotex, Inc. ("Apotex"). This case arises from patent infringement litigation involving four patents generally directed to treatment methods with the drug varenicline: U.S. Patent Nos. 9,504,644 (the '644 patent"), 9,504,645 (the '"645 patent"), 9,532,944 (the '944 patent"), and 9,597,284 (the '284 patent"). Plaintiff Oyster Point owns these patents and has sued the Defendant for patent infringement under the Hatch-Waxman Act. The parties seek claim construction of one term in these patents.

ANALYSIS

I. The law of claim construction

A court's determination "of patent infringement requires a two-step process: first, the court determines the meaning of the disputed claim terms, then the accused device is compared to the claims as construed to determine infringement." Acumed LLC v. Stryker Corp., 483 F.3d 800, 804 (Fed. Cir. 2007). "[W]hen the district court reviews only evidence intrinsic to the

patent (the patent claims and specifications, along with the patent's prosecution history), the judge's determination will amount solely to a determination of law." Teva Pharms. USA, Inc. v. Sandoz, Inc., 135 S. Ct. 831, 841 (2015).

The focus of claim construction is the claim language itself:

> It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude. Attending this principle, a claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to 'particularly point[] out and distinctly claim[] the subject matter which the patentee regards as his invention.'

Innova/Pure Water, Inc. v. Safari Water Filtration Sys., 381 F.3d 1111, 1115-1116 (Fed. Cir. 2004) (citations omitted).

The Federal Circuit has established this framework for the construction of claim language:

> We have frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.' We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application. The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation. . .
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> In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean. Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning

> relevant scientific principles, the meaning of technical terms, and the state of the art.

Phillips v. AWH Corp., 415 F.3d 1303, 1312-1314 (Fed. Cir. 2005) (citations omitted).

II. Claim construction of the disputed terms

A. "Non-systemically bioavailable dose"

This case concerns ten patents directed to the use of a varenicline nasal spray to treat dry-eye disease ("DED"). In the four patents presented for claim construction ('644, '645, '944, and '284), independent claim 1 requires local administration of "non-systemically bioavailable dose" amounts of varenicline. The parties dispute the meaning of the claim term, "non-systemically bioavailable dose." Plaintiff contends that the phrase has its plain and ordinary meaning, which is "dose that does not result in systemically bioavailability in a pharmacologically relevant concentration." Defendant contends that this phrase means, "dose that remains in the nasal mucosa and does not enter systemic circulation."

This claim construction dispute is somewhat unusual because, in the briefs, the parties do not dispute the meaning of the words, "systemically bioavailable" or "dose" in the phrase, "non-systemically bioavailable dose." Instead, the sole matter in dispute appears to be whether "non" means "not at all" or, similarly, "none whatever." Defendant contends that the claim term requires that none of the active ingredient enter the bloodstream after administration (such that none whatever becomes systemically bioavailable.) Plaintiff contends that "non" means "not in any relevant amount." Thus, according to Plaintiff, the claim term does not require that none of the active ingredient enter the bloodstream. The Court thus limits the inquiry to the question of whether the term at issue requires that none of the dose whatever enters the bloodstream after administration.

Plaintiff argues that its position is consistent with the remaining language in three out of four of the claims at issue,[1] while Defendant's position conflicts with another limitation in those claims. Claim 1 of the '644 patent is representative of that group of three independent claims:

> 1. A method of increasing tear production, comprising the local administration of a therapeutically effective amount of a nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor, is varenicline administered in a non-systemically bioavailable dose between 5 micrograms and 50 micrograms per dose, and does not cross the blood-brain barrier in a pharmacologically relevant concentration.

Plaintiff points to the terminal claim limitation, "and does not cross the blood-brain barrier in a pharmacologically relevant concentration" ("the Barrier Phrase.") Plaintiff argues, in short, that Defendant's position renders this phrase superfluous, since, if none of the dose of the active whatever enters the bloodstream, it is impossible for that dose to cross the blood-brain barrier, making the Barrier Phrase claim limitation meaningless.

In response to this argument, Defendant argues that "to the extent this language is superfluous under Apotex's construction it is equally superfluous under Oyster Point's construction." (D.'s Resp. Br. at 5.) Even if the Court agreed with Defendant on this point, it, at most, points out a problem with Plaintiff's proposed construction; it does not effectively rebut Plaintiff's critique of Defendant's proposed construction. Defendant does not otherwise address the point that its proposed construction renders the Barrier Phrase of claim 1 (in three of four patents) superfluous.

The Federal Circuit recently addressed a similar problem in Voice Tech. Corp. v. Unified

[1] Only claim 1 of the '645 patent lacks the Barrier Phrase claim limitation that appears in independent claim 1 in each of the three other patents at issue. Neither party contends that this fact should alter the construction of "non-systemically bioavailable dose" in the '645 patent.

Pats., LLC, 110 F.4th 1331, 1342-43 (Fed. Cir. 2024). In Voice Tech., the Court rejected an interpretation of a claim term that would render superfluous another term in the same claim. Id. In support of the interpretive principle, the Court cited two cases:

> *See SimpleAir, Inc. v. Sony Ericsson Mobile Commc'ns AB*, 820 F.3d 419, 429 (Fed. Cir. 2016) ("[I]nterpretations that render some portion of the claim language superfluous are disfavored." (internal quotation marks and citation omitted)); *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so.").

Id. at 1343.[2]

The Court thus finds that Apotex has proposed a construction that is disfavored under Federal Circuit law. The Court next inquires: what intrinsic evidence does Apotex cite in support of its position? Apotex begins by arguing that "non-systemically" is a clear statement that "the dose of varenicline does ***not*** enter the systemic circulation following administration into the nose." (Def.'s Br. at 11.) The Court agrees in very small part that the phrase, "non-systemically," appears to have a plain meaning that something is not done in a systemic manner, but this is a long way from shedding light on the meaning of "non-systemically bioavailable dose" in the context of this claim. The Court does not agree that it is plain from the words themselves that "non-systemically" means "does not enter the bloodstream." Defendant's first argument is mere insistence that they are obviously correct, but the Court has not been persuaded.

[2] In support of its superfluousness argument, Plaintiff cited Phillips, 415 F.3d at 1325, but the cited section does not make clear that a construction of one term in a claim that renders superfluous another term in that same claim is disfavored. Voice Tech. makes clear that this interpretive principle applies to terms within the same claim, and not just between different claims.

Apotex next argues that its construction is supported by the absence of the phrase, "in a pharmacologically relevant concentration," as a modifier of "non-systemically bioavailable dose." Apotex contends that the absence of that qualifier is evidence that "does not enter the bloodstream" is implied with regard to the "non-systemically bioavailable dose." The Court does not follow the reasoning here and is not persuaded that the absence of the phrase, "in a pharmacologically relevant concentration," as a modifier of "non-systemically bioavailable dose," is evidence that "does not enter the bloodstream in any amount" is implied as an attribute of the dose.

Apotex next offers a statement from the examiner during prosecution of the '284 patent. Statements by the examiner do not constitute intrinsic evidence of the applicants' understanding of the meaning of claim terms. The Federal Circuit has held: "Although prosecution history can be a useful tool for interpreting claim terms, it cannot be used to limit the scope of a claim unless the applicant took a position before the PTO that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter." Schwing Gmbh v. Putzmeister Aktiengesellschaft & Putzmeister, 305 F.3d 1318, 1324 (Fed. Cir. 2002). Apotex has not pointed to evidence of a position taken by the applicants during prosecution, nor offered authority to support its use of an examiner statement.[3] Furthermore, Apotex has not pointed to any evidence that the applicants disclaimed coverage of varenicline nasal spray treatments in which the active merely entered the bloodstream (as opposed to treatments in which the

[3] Under Federal Circuit law, "the statements of an examiner will not necessarily limit a claim." Bell Atl. Network Servs. v. Covad Communs. Grp., 262 F.3d 1258, 1273 (Fed. Cir. 2001). While this phrasing suggests the possibility that an examiner statement may be found to limit a claim, Defendant has made no showing that, in this case, such an inference is permissible.

therapeutic effect resulted from systemic circulation.)

The Court finds that Apotex has offered no intrinsic evidence which supports its position.

In support of its position, Plaintiff begins with the language of claim 1 of three of the four patents, already described. The Court agrees with Plaintiff that the terminal limitation, "does not cross the blood-brain barrier in a pharmacologically relevant concentration," is superfluous unless some of the administered dose might enter the bloodstream. As Plaintiff contends, the terminal limitation "only makes sense" if some varenicline may enter the blood. (Pl.'s Br. at 15.) This is important evidence that supports Plaintiff's interpretation of the claim language at issue.

Next, Plaintiff points to some of the claims that depend from claim 1. For example, claim 4 of the '644 patent states:

> 4. The method of claim 1, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor in an amount that does not result in undesired systemic side effects.

Plaintiff contends that this claim would be superfluous if no varenicline entered systemic circulation, and is only meaningful if some varenicline does so. The Court agrees.

Plaintiff argues that the prosecution history confirms its understanding of the claim term at issue. The Court finds that, in fact, the prosecution history of the '644 patent sheds a great deal of light on the patentees' understanding of the claim term at issue.[4] As originally drafted, the relevant claims stated:

> 1. A method of increasing tear production, comprising the local administration of a therapeutically effective amount of a nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor.

[4] The prosecution history documents cited in the discussion that follows were obtained through the PTO's online search tool, "Patent Center," publicly available at "https://patentcenter.uspto.gov/."

2. The method of claim 1, wherein the agonist does not cross the blood-brain barrier in a pharmacologically relevant concentration.
3. The method of claim 1, wherein the agonist selectively binds to at least one of the peripheral nicotinic acetylcholine receptor subtypes selected from alpha3beta4, alpha4beta2, and alpha7.
4. The method of claim 1, wherein the agonist is administered in an amount that is not systemically bioavailable.

("Claims," dated 10/19/2015.) In the first office action, the PTO rejected claims 1 through 6 under 35 U.S.C. § 103 as being unpatentable over Ziegler in view of Yerxa. ("Non-final Rejection," dated 3/26/2016, at 3.) In brief, the examiner explained that Ziegler taught the administration of a pharmaceutical formulation comprising varenicline, administered into the nasal cavity, and that Yerxa taught that intranasal administration of nicotinic acetylcholine receptor agonists is useful for treating DED; therefore, it would have been obvious to use the method of Ziegler to treat DED. (Id. at ¶ 4.)

In response to the office action, the applicants submitted amended claims and remarks. ("Claims," "Applicant Arguments," both dated 6/24/2016.) The applicants submitted an amended claim 1, with the new matter underlined:

> 1. (Currently Amended) A method of increasing tear production, comprising the local administration of a therapeutically effective amount of a nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor, is administered in an amount that is not systemically bioavailable, and does not cross the blood-brain barrier in a pharmacologically relevant concentration.

("Claims," dated 6/24/2016.) In the remarks, the applicants stated:

> The current pending application solves problems identified by the inventors for increasing tear production with the intranasal administration of nicotinic acetylcholine receptor agonists. To avoid the issues associated with a) systemic exposure of nicotinic acetylcholine receptor agonists, and b) receptor desensitization, the methods described herein are directed to the local administration of a nicotinic acetylcholine receptor agonist into the nasal cavity

> whereby a non-systemic dose of the agonist achieves a high concentration in the nasal cavity for a short period of time and binds to the peripheral nicotinic acetylcholine receptor. *In this manner, side effects associated with systemic exposure of the nicotinic acetylcholine receptor agonist to the CNS are eliminated, and the transient nature of the agonist exposure minimizes receptor desensitization. Hence, the local and transient effect of the nicotinic acetylcholine receptor agonist in the nasal cavity is sufficient to provide therapeutic relief (e.g., increasing tear production) while not being systemically bioavailable in any relevant amount.*
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> Indeed, the therapeutic benefit (e.g., increasing tear production) of a locally administered, nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor, is administered in an amount that is not systemically bioavailable, and does not cross the blood- brain barrier in a pharmacologically relevant concentration has not been disclosed previously. . . . In contrast to Applicant's discovery, none of these references describe the therapeutic benefit of a non-systemically bioavailable nicotinic agonist locally administered into the nasal cavity that selectively binds to the peripheral nicotinic acetylcholine receptor.

("Applicant Arguments," dated 6/24/2016, at 4-5 (italics added.) The applicants continued with a discussion of the teachings of Ziegler and Yerxa:

> Ziegler teaches a method for reducing nicotine addiction or aiding in the cessation or lessening of tobacco use in a subject. . . . Furthermore, since nicotine dependence is mediated by nicotinic acetylcholine receptor agonists in the brain, a person of skill in the art would understand that any pharmacotherapy taught by Ziegler would require systemic bioavailability to act on the central nervous system. Thus, the methods taught by Ziegler are directed to systemically bioavailable varenicline. . .
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> Yerxa issued claim 12 recites, "wherein said systemic administration involves administration of a liquid/liquid suspension of said compound via nose drops or nasal spray, or administration of a nebulized liquid to oral or nasopharyngeal airways of said subject, such that a therapeutically effective amount of said compound contacts lacrimal tissues of said subject via systemic absorption and circulation." Hence, similar to the methods taught by Ziegler, Yerxa is also directed to a systemically bioavailable nicotinic acetylcholine receptor agonist. . .
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> The instant claims are directed to a method of increasing tear production, comprising the local administration of a therapeutically effective amount of a nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in

> need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor, is administered in an amount that is not systemically bioavailable, and does not cross the blood-brain barrier in a pharmacologically relevant concentration. Consequently, the instantly claimed method is to a non-systemic administration of a nicotinic acetylcholine receptor agonist, thereby devoid of untoward CNS effects. In contrast, as discussed above, Ziegler and Yerxa are directed to a systemically administered, bioavailable nicotinic acetylcholine receptor agonist wherein the agonist acts on the CNS. Therefore, a person of skill in the art would not derive the methods of the instant claims of increasing tear production with a locally administered, non-systemically bioavailable nicotinic acetylcholine receptor agonist based on Ziegler and Yerxa which teach a systemically administered, bioavailable nicotinic acetylcholine receptor agonist that acts on the CNS.

(Id. at 5-7.)

On September 29, 2016, the PTO issued a Notice of Allowance. ("Notice of Allowance," dated 9/29/2016.) Together with the Notice, the examiner issued various comments. In a subsection titled "Rejoinder," the examiner stated: "the point of patentability is the intranasal administration of varenicline sub-systemic doses." (Id. at 2.) The examiner then stated that claim 1 had been amended by the examiner with the authorization of the applicants, and showed the amendment:

> Claim 1. (Currently Amended) A method of increasing tear production, comprising the local administration of a therapeutically effective amount of a nicotinic acetylcholine receptor agonist into the nasal cavity of an individual in need thereof, wherein the agonist selectively binds to the peripheral nicotinic acetylcholine receptor, is varenicline administered in ~~an amount that is not systemically bioavailable~~ a non-systemically bioavailable dose between 5 micrograms and 50 micrograms per dose, and does not cross the blood-brain barrier in a pharmacologically relevant concentration.

(Id. at 3.) Under "Examiner's Statement of Reasons for Allowance," the examiner stated:

> Applicant's arguments have overcome the rejections of record . . . In particular, none of the references applied teach or suggest a nonsystemic local dose of varenicline for intranasal administration.

(Id. at 4.)

One statement from the prosecution history is most relevant to the claim construction issue presently before the Court. Plaintiff points to this statement:

> Hence, the local and transient effect of the nicotinic acetylcholine receptor agonist in the nasal cavity is sufficient to provide therapeutic relief (e.g., increasing tear production) while not being systemically bioavailable in any relevant amount.

("Applicant Arguments," dated 6/24/2016, at 4.) The Court agrees with Plaintiff that this statement is very clear evidence that the applicants did not understand "non-systemically bioavailable dose" to mean none of the dose whatever becomes systemically bioavailable. The statement shows that the applicants understood that some amounts of the dose of the active may enter the bloodstream.

Defendant argues that the prosecution history supports its proposed construction, but the Court is not persuaded. Defendant contends that the statement just discussed, the "any relevant amount" statement, should be taken as evidence that the absence of "in any relevant amount" in the claim language was knowing and intentional. The Court is not persuaded by this reasoning and finds that the "any relevant amount" statement means what it says: the applicants understood the administered dose to be not systemically bioavailable in any relevant amount, rather than not at all systemically bioavailable. Defendant's attempt to turn that statement on its head is not persuasive.

Furthermore, the Court finds nothing in the "Applicant Arguments" document that distinguishes the invention from the prior art based on the invention's active *never* entering the bloodstream. Nor does Defendant point to any specific statements by the applicants in the prosecution history in which they clearly distinguished the prior art on the basis of whether or

not the active ingredient ever entered the bloodstream.[5] There is no evidence that the applicants made the distinction that Defendant proposes. To the contrary, we find in the prosecution history a clear statement that the applicants understood "not systemically bioavailable," as applied to the administered dose, to mean, "not systemically bioavailable in any relevant amount."

The Court agrees with Plaintiff that "non-systemically bioavailable dose" does not mean that the claim requires that none whatever of the dose of the active enters the bloodstream. The Court finds that Defendant's position is unsupported by the intrinsic evidence. Yet the Court does not today adopt either party's construction of the claim term at issue. Defendant's proposed construction is not supported by the intrinsic evidence. But Plaintiff's proposed construction creates interpretive problems. First, it is circular, defining "non-systemically bioavailable dose" by recycling the phrase, "systemic bioavailability," which neither party has defined. Second, and more importantly, it introduces a new ambiguity by adding the phrase, "pharmacologically relevant concentration." In the absence of any definition of "relevant," this is too ambiguous to serve as part of the end product of a Markman inquiry.[6]

Fortunately, it does not appear that the parties need the Court to choose a phrase to

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[5] Instead, the applicants amended claim 1 with the phrase that eventually became, "non-systematically bioavailable dose," in order to distinguish the Ziegler and Yerxa references. In doing so, the applicants distinguished Ziegler and Yerxa as being treatments that achieved a therapeutic effect by means of systemic circulation, while the inventive treatment did not achieved a therapeutic effect by means of systemic circulation.

[6] To start with, Plaintiff's use of the phrase leaves open the question of what "relevant" would mean in the proposed construction: relevant to what? Consider how the phrase appears in claim 1 in the Barrier Phrase claim limitation, "does not cross the blood-brain barrier in a pharmacologically relevant concentration." In that phrase, one perhaps might expect that the concentration is relevant to the effects of crossing the blood-brain barrier and possible CNS side effects that result. In Plaintiff's proposed construction, it is unclear what defines a relevant concentration or how one would ascertain that. In short, including that phrase opens a new can of worms.

resolve the dispute they have presented: it is enough to determine that "non-systemically bioavailable dose" does not require that none of the dose whatever enter the bloodstream. Defendant's position on this issue is unsupported by the intrinsic evidence. Should either party find that this resolution is insufficient and that further construction is needed, it may be requested.

In conclusion, the Court determines that "non-systemically bioavailable dose" does not require that none of the dose of the active enters the bloodstream.

SO ORDERED.

s/ Stanley R. Chesler
STANLEY R. CHESLER, U.S.D.J.

Dated: October 1, 2024